

NaY Zeolite: A Useful Catalyst for Nitrile Hydrolysis

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Abstract: The NaY zeolite catalysed hydrolysis of nitriles to primary amides is reported. It is found that aryl nitriles with strong electron-withdrawing substituents and cyanopyridines are readily hydrolysed in the water suspension, while aliphatic nitriles do not react.

Keywords: NaY zeolite, aromatic nitriles, solvolysis.

Introduction

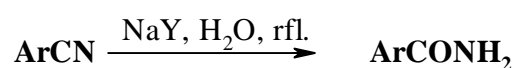
Zeolites are effective catalysts in organic chemistry and their specificity in gas phase transformations is greatly utilised in industry [1]. Alkylation reaction, polymerisation, cyclization [2], photoreduction [3], or preparation of nitroalkenes [4], occur in gas phase or with reactants sorbed within zeolite in inert solvent. Recently, several reports on the use of acidic zeolites (HY) in macrolactonization [5], acetalization [6], acetylation [7] and *gem*-diacetalization [8], as well as the synthesis and application of the first organic-functionalized zeolite-beta [9], prompted us to investigate the new catalytic possibilities of NaY zeolite.

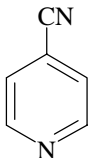
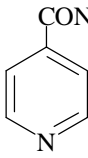
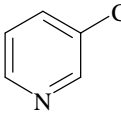
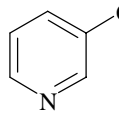
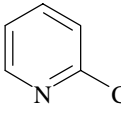
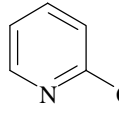
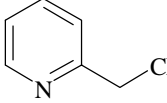
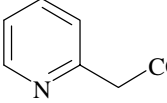
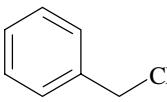
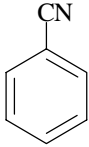
Here we wish to report the application of NaY zeolite as reusable catalyst in the hydrolysis of nitriles to primary amides.

Results and Discussion

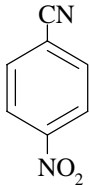
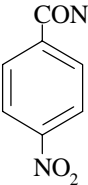
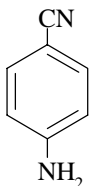
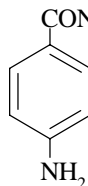
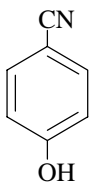
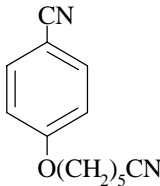
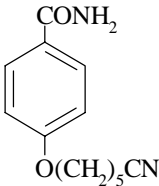
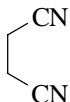
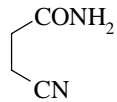
In our experiments the suspension of NaY zeolite and a nitrile in water (or methanol) was heated to reflux for a given period (Table 1), zeolite was filtered off, and products were separated (or directly crystallised). Most important observation is that nitriles are hydrolysed only to the amide stage. Cyanopyridines and benzonitriles with electron-withdrawing substituents are readily hydrolysed in good yield (Table 1, entries 1-3, 7).

Table 1. Hydrolysis of nitriles into amides^a.



| Entry | Nitrile | Time (h) | Yield (%) ^b | Amide |
|-------|---|----------|---------------------------------|--|
| 1 |  1 | 24 | 87 |  2 |
| | | 14 | 76 | |
| | | 6 | 67 | |
| 2 |  3 | 24 | 86 (84, 80, 82) ^c |  4 |
| 3 |  5 | 24 | 92 |  5 |
| 4 |  7 | 48 | 16 |  8 |
| 5 |  9 | 48 | NR ^d | |
| 6 |  10 | 48 | NR | |

Continuation of the Table 1.

| Entry | Nitrile | Time (h) | Yield (%) ^b | Amide |
|-------|---|----------|------------------------|---|
| 7 |  11 | 24 | 87 |  12 |
| 8 |  13 | 48 | 35 |  14 |
| 9 |  15 | 48 | NR | |
| 10 |  16 | 48 | 21 |  17 |
| 11 |  18 | 24 | 35 |  19 |
| 12 | NCCH ₂ CH ₂ CO ₂ Et (20) | 2 | quant. | NCCH ₂ CH ₂ CO ₂ H (21) |

^a NaY / nitrile = 4 : 1 (w / w). ^b Yield of isolated compounds. ^c Yield of nicotinamide (**4**) with reused NaY zeolite. ^d No reaction.

Benzonitrile (**10**, entry 6) was totally resistant to hydrolysis, while benzonitriles substituted with weak inductive electron-withdrawing groups (with strong +R, 4-aminobenzonitrile (**13**) and 4-(5-cyanopentoxy)benzonitrile (**16**) [10], Table 1, entries 8 and 10) were hydrolysed, although in low yield (35% and 21%, respectively). Hydroxy substituent completely prevented the hydrolysis (**15**, Table 1, entry 9) probably as a consequence of phenoxy ion formation. The case of di-nitrile **16** is very inter-

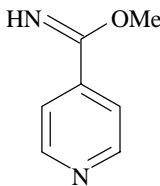
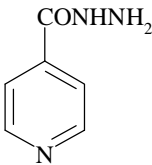
esting: it shows that hydrolysis proceeds by blocking the formation of phenoxy ion, while at the same time pointing to the resistance of aliphatic nitriles to hydrolysis. The resistance of aliphatic nitriles was confirmed by attempted hydrolysis of CH_3CN (not shown) and by hydrolysis of ethyl 3-cyanopropanoate **20** only to cyanoacid **21** (Table 1, entry 12). Benzylic cyano group was also found to be resistant to applied conditions (**9**, Table 1, entry 5), or was very slightly hydrolysed when CH_2CN was attached to the electron-withdrawing pyridine ring (**7** \rightarrow **8**, 16%, Table 1, entry 4).

Hydrolysis of succinodinitrile (**18**, Table 1, entry 11) afforded only 35% of 2-cyanopropanamide (**19**) and 65% of educt. It is interesting to note that much greater site-differentiation was achieved in enzymatic hydrolysis of α,ω -dinitriles into corresponding ω -cyanoacids [11].

In some cases, prolonged reaction time resulted in higher yields, as is given for 4-cyanopyridine (**1**) (Table 1, entry 1, 6 h (67%) \rightarrow 24 h (87%)). The reusability of NaY catalyst was tested using 3-cyanopyridine (**3**, Table 1, entry 2). Four runs were performed with the same batch of the catalyst without significant loss of its activity.

In Table 2 the influence of reactant (solvent) is shown. Using methanol instead of water the imino ester **22** was obtained in good yield (67%; entry 2), while ethanol and higher homologues (propanol and 1-butanol) were ineffective. However, hydrazine hydrate afforded isoniazide (**23**, 67%) along with 18% of isonicotinamide (**2**).

Table 2. Solvolysis of 4-cyanopyridine (**1**).

| Entry | Reactant [time (h)] | Product | Yield (%) ^a |
|-------|--|---|------------------------|
| 1 | H_2O (24) | isonicotinamide (2) | 87 |
| 2 | CH_3OH (14) |  22 + isonicotinamide (2) | 67 12 |
| 3 | ethanol (10) propanol (10) 1-butanol (10) | NR | |
| 4 | $\text{NH}_2\text{NH}_2 \times \text{H}_2\text{O}$ (2) |  23 + isonicotinamide (2) | 67 18 |

^a Yield of isolated compounds.

The influence of the amount of catalyst on product distribution is exemplified with methanolysis of 4-cyanopyridine (**1**) (Table 3). Product formation started with 6% (w/w) of catalyst, and the increase of zeolite part did not significantly affect the product distribution, what, beside its already shown reusability, confirms the true catalytic nature of NaY zeolite.

Table 3. Methanolysis of 4-cyanopyridine (**1**): dependence on catalyst-to-substrate ratio (reflux 15 h).

| Entry | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---------------------------------|---------|---------|---------|---------|---------|---------|---------|
| NaY / 1 (w/w) | 4 | 2 | 1 | 0.5 | 0.2 | 0.1 | 0.06 |
| 22 / 1 (GC ratio) | 73 : 27 | 65 : 35 | 63 : 35 | 60 : 38 | 61 : 32 | 66 : 32 | 51 : 47 |

Conclusion

We have shown that NaY zeolite can be used in the simple procedure as a reusable catalyst for hydrolysis of aromatic nitriles, primarily of cyanopyridines and benzonitriles possessing electron-withdrawing groups. Contrary to hydrolysis under acidic conditions, benzyl- and alkanenitriles are stable under conditions applied, so enabling their further selective transformations. In addition, NaY zeolite can also be used for imino ester preparation as an alternative to Pinner synthesis.

Experimental

General

Melting points were determined on a Mikro-Heiztisch Boetius PHMK apparatus and were not corrected. IR spectra were recorded on Perkin-Elmer spectrophotometer FT-IR 1725X. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini-200 or Bruker AM-250 spectrometers. Chemical shifts were expressed as ppm (δ) values and coupling constants (J) in Hz. Mass spectra were taken on a Finnigan-MAT 8230 spectrometer, as indicated below.

In our experiments, NaY zeolite with following characteristics was used [12]: crystallinity 100%; SiO_2 [%] 63.80; Al_2O_3 [%] 22.90; NaO [%] 13.30; molar ratio SiO_2 / Al_2O_3 : 4.73; specific area (B.E.T) $850 \text{ m}^2 / \text{g}$; pore volume $0.32 \text{ cm}^3 / \text{g}$; diameter of crystallite $3.5 \mu\text{m}$; diameter of granulate $150 \mu\text{m}$; pH of water suspension 10.05. Zeolite was pre-dried only for methanolysis reaction, in order to suppress the formation of an amide, and for acetylation reactions.

Hydrolysis of Nitriles - General

The suspension of a nitrile (200 mg) and zeolite (800 mg) in water (5 ml) was heated to reflux (for details see Table 1). The hot reaction mixture was filtered and zeolite was washed with water (and/or

methanol). When catalyst was reused, it was dried on air overnight. Pure amides were crystallised directly from the crude product mixture or were purified by column chromatography (SiO₂ or RP-18). All isolated compounds were fully characterised by spectroscopic and analytical methods.

The data of known compounds were compared with literature data given in [13], and that refers to:

2: mp 152-154°C, [14] mp 155-157°C

4: mp 128-129°C, [13, p. C-474] mp. 129-131°C

6: mp 106-108°C, [13, p. C-474] mp 107-108°C

12: mp 201-202.5°C, [13, p. C-197] mp 201.4°C

14: mp 184-186°C, [13, p. C-183] mp 183°C

21: mp 48-50°C, [11] mp 49.5-51°C.

2-Pyridylacetamide (**8**)

Mp 120-121°C. (colourless needles, water). IR (KBr) cm⁻¹: 3377, 3188, 3112, 3017, 1678, 1646, 1597, 1570, 1439, 1402. ¹H NMR (CD₃OD, 200 MHz): 8.51-8.43 (m, 1H, H-C(6')), 7.78 (td, *J* = 7.8, 1.8, H-C(4')), 7.40 (d, *J* = 8.0, H-C(3')), 7.30 (ddd, *J* = 8, 5, 1, H-C(5')), 3.75 (s, 2H-C(2)). ¹³C NMR (CD₃OD, 50 MHz): 174.97 (C1), 156.82 (C2'), 149.86 (C6'), 138.76 (C4'), 125.69 (C3'), 123.59 (C5'), 45.12 (C2). Anal. calc. for C₇H₈N₂O (136.06): C 61.75, H 5.92, N 20.57, found: C 62.08, H 5.57, N 20.83.

3-Cyanopropanamide (**19**)

Mp 86-88°C (colourless amorphous solid). IR (KBr) cm⁻¹: 3414, 3225, 2293, 2248, 1681, 1619, 1421. ¹H NMR (D₂O, 200 MHz) δ: 2.80-2.65 (m, 4H, 2H-C(2), 2H-C(3)). ¹³C NMR (D₂O, 50 MHz) δ: 177.90 (C1), 123.04 (C4), 32.38 (C2), 15.12 (C3). MS (CI, isobutane): 197 (2 M⁺+1). Anal. calc. for C₄H₆N₂O (98.11): C 48.97, H 6.16, found: C 49.34, H 6.08.

4-(5-Cyanopentoxy)benzamide (**17**)

Colourless solid mp 97-101°C. IR (KBr) cm⁻¹: 3466, 2140, 1614, 1566, 1401. ¹H NMR (CD₃OD, 200 MHz): 7.84 (AA'BB', *J* = 6.8, 2, H-C(2), H-C(6)), 6.98 (AA'BB', *J* = 6.8, 2, H-C(3), H-C(5)), 4.06 (t, *J* = 6.2, 2H-C(1')), 2.49 (t, *J* = 6.8, 2H-C(5')), 1.90-1.57 (m, 6H). MS (EI, 70 eV): 232 (M⁺, 25), 137 (33), 121 (100), 96 (14), 55 (8), 41(5). Anal. calc. for C₁₃H₁₆N₂O₂ (232.12): C 67.22, H 6.94, N 12.06, found: C 67.54, H 6.90, N 12.54.

Iminoester **22**

The suspension of 4-cyanopyridine (**1**, 200 mg) and zeolite (800 mg) in methanol (5 ml) was heated to reflux for 14 h. Hot reaction mixture was filtered and zeolite was washed with methanol. Crude

product was chromatographed on Lobar RP-18 column (eluent: CH₃OH / H₂O = 40 : 60) affording the analytical sample of iminoester **22** (175 mg, 67%), isonicotinamide (**2**, 28 mg, 12%) and educt **1** (36 mg, 18%). **22**: mp = 45°C (colourless needles, diisopropyl ether). IR (KBr) cm⁻¹: 3290, 3220, 3034, 1651, 1603, 1556, 1445, 1348, 1313, 1108, 1087. ¹H NMR (200 MHz, DMSO-*d*₆): δ 9.50 (bs, HN=C), 8.76 (AB, *J* = 4, H-C(2), H-C(6)), 7.80 (AB, *J* = 4, H-C(3), H-C(5)), 3.82 (s, CH₃O-). ¹³C NMR (50 MHz, DMSO-*d*₆, DEPT): δ 164.14 (C=N), 150.60 (C2 and C6), 138.82 (C4) 121.08 (C3 and C5), 53.46 CH₃. MS CI (isobutane): 137 (MH⁺). Anal. calc. for C₇H₈N₂O (136.15): C 61.75, H 5.92, N 20.57, found: C 62.04, H 5.89, N 19.96.

Isoniazid (**23**)

The suspension of 4-cyanopyridine (**1**, 1.00 g) and zeolite (1.00 g) in hydrazine hydrate (1.00 ml) and water (8 ml) was heated at 90°C for 2 h. Hot reaction mixture was filtered and zeolite was washed with hot ethanol. Crude product crystallised affording 478 mg of **23**, and the rest was chromatographed on SiO₂ column (eluent: methanol / EtOAc (1:9)). Isoniazid (**23**) was obtained in combined yield of 67% (883 mg), together with 211 mg (18%) of isonicotinamide (**2**). **23**: mp 169°C (colourless needles, ethanol). [13, p. C-475] mp 171-173°C. IR (KBr) cm⁻¹: 3111, 3050, 1667, 1635, 1557. ¹H NMR (DMSO-*d*₆, 250 MHz): 10.13 (s, 1H), 8.76-8.67 (m, 2H, H-C(2), H-C(6)), 7.80-7.68 (m, 2H, H-C(3), H-C(5)), 4.77-4.60 (m, 2H). ¹³C NMR (DMSO-*d*₆, 62.5 MHz): 164.02 (C=O), 150.26 (C2 and C6), 140.30 (C4), 121.06 (C3 and C5). Anal. calc. for C₆H₇N₃O (137.17): C 52.54, H 5.15, N 30.64; found: C 52.31, H 5.27, N 30.83.

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References and Notes

1. Hölderich, W.; Hesse, M.; Naumann, F. Zeolites: catalysts for organic synthesis. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 226-246.
2. Sen, S. E.; Zhang, Y. Z.; Roach, S. L. Zeolite-mediated cyclization of an epoxide-containing polyene. *J. Org. Chem.* **1996**, *61*, 9534-9537.
3. Rao, J. V.; Uppili, S. R.; Corbin, D. R.; Schwarz, S.; Lustig, S. R.; Ramamurthy, V. Facial selective photoreduction of steroids: role of zeolites. *J. Am. Chem. Soc.* **1998**, *120*, 2480-2481.
4. Sreekumar, R.; Padmakumar, S. R.; Rugmini, P. Regioselective reduction of epoxides and conjugated carbonyl compounds using zeolite supported zinc borohydride. *Tetrahedron Lett.* **1998**, *39*, 5151-5154.
5. a) Ookishi, T ; Onaka, M. Zeolite-catalyzed macrolactonization of ω-hydroxyalkanoic acids in a

- highly concentrated solution. *Tetrahedron Lett.* **1998**, *39*, 293-296; b) Tatsumi, T.; Sakashita, H.; Asanao, K. Selective macrolactonization using zeolite molecular sieves. *J. Chem. Soc., Chem. Commun.* **1993**, 1264-1265.
6. a) Ballini, R.; Bosica, G.; Frullanti, B.; Maggi, R.; Sartori, G.; Schroer, F. 1,3-Dioxolanes from carbonyl compounds over zeolite HSZ-360 as a reusable, heterogenous catalyst. *Tetrahedron Lett.* **1998**, *39*, 1615-1618; b) Corma, A.; Climent, M. J.; Carcia, H.; Primo, J. *Applied Catalysis* **1990**, *59*, 333-340.
 7. Ballini, R.; Bosica, G.; Carloni, S.; Ciaralli, L.; Maggi, R.; Sartori, G. Zeolite HSZ-360 as a new reusable catalyst for the direct acetylation of alcohols and phenols under solventless conditions. *Tetrahedron Lett.* **1998**, *39*, 6049-6052.
 8. Ballini, R.; Bordoni, M.; Bosica, G.; Maggi, R.; Sartori, G. Solvent free synthesis and deprotection of 1,1-diacetates over a commercially available zeolite Y as a reusable catalyst. *Tetrahedron Lett.* **1998**, *39*, 7587-7590.
 9. a) Jones, C. W.; Tsuji, K.; Davis, M. E. Organic-functionalized molecular sieves as shape-selective catalysts. *Nature* **1998**, *393*, 52-54; b) Creighton, E. J. Organic groups cling to the pores. *Nature* **1998**, *393*, 21-22.
 10. The structure of 4-(5-cyanopentoxy)benzamide (**17**) was deduced (beside IR and microanalytical data) by comparison of its spectral data with that of **16** (*vide infra*). ¹H NMR: replacing of CN group with CONH₂ on benzene ring leads to downfield shift of *ortho*-protons (0.25 ppm) and small upfield shift of *meta*-protons (-0.08 ppm), what is in good agreement with observed values (0.25 and -0.04 ppm, respectively). Source: Pretsch, E.; Clerc, T.; Seibl, J.; Simon, W. *Tabellen zur Strukturaufklärung organischer Verbindungen*, 3rd Ed.; Springer-Verlag: Berlin - Heidelberg - New York - Tokyo, 1986; p H260. Also, in mass spectra of both compounds cyanoalkyl chain and McLafferty rearrangement could be observed (m/e 96 and 41, respectively). Data for 4-(5-cyanopentoxy)benzonitrile (**16**): colourless oil. ¹H NMR (CDCl₃, 200 MHz): 7.59 (AA'BB', *J* = 6.8, 2, H-C(2), H-C(6)), 6.94 (AA'BB', *J* = 6.8, 2, H-C(3), H-C(5)), 4.03 (t, *J* = 6.2, 2H-C(1')), 2.41 (t, *J* = 6.8, 2H-C(5')), 1.93-1.56 (m, 6H). ¹³C NMR (CDCl₃, 50 MHz): 162.13 (C4), 133.99 (C2 and C6), 119.97 (CN), 119.20 (CN), 115.09 (C3 and C5), 103.89 (C1), 67.66 (C1'), 28.19, 25.20, 25.04, 17.08 (C5'). MS (EI, 70 eV): 215 (44), 214 (M⁺, 95), 119 (100), 96 (35), 55 (22), 41 (39). Anal. calc. for C₁₃H₁₄N₂O (214.11): C 72.87, H 6.59, found: C 72.96, H 6.87.
 11. Gavagan, J. E.; Fager, S. K.; Fallon, R. D.; Folsom, P. W.; Herkes, F. E.; Eisenberg, A.; Hann, E. C.; DiCosimo, R. Chemoenzymatic production of lactams from aliphatic α,ω-dinitriles. *J. Org. Chem.* **1998**, *63*, 4792-4801.
 12. Stojković, S.; Gajinov, S.; Adnađević, B. Correlation between a degrees of crystallinity of acid treated NaA and NaY zeolites as determined by infrared and X-ray diffraction. *Spectroscopy Lett.* **1991**, *24*, 801-815.

13. *CRC Handbook of Chemistry and Physics*, 57th Ed.; CRC Press Inc.: Cleveland, Ohio, 1976-1977.
14. *Beilstein Handbuch Der Organischen Chemie*; Springer-Verlag: Berlin - Göttingen - Heidelberg, 1953; E-II, 22, 37.

Samples Availability: Available from the authors.

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